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New insights on growth trajectory in infants with complex congenital heart disease

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ABSTRACT

Purpose: We aimed to describe the weight-for-age *Z*-score growth trajectory (WAZ-GT) of infants with complex congenital heart disease (cCHD) after neonatal cardiac surgery in the first 4 months of life and assess potential risk factors.

Methods: We utilized data from a previously reported trial of the REACH telehealth home monitoring (NCT01941667) program which evaluated 178 infants with cCHD from 2012 to 2017. Over the first 4 months of life, weekly infant weights were converted to WAZ. WAZ-GT classes were identified using latent class growth modeling. Multinomial logistic regression models were used to examine the associations between potential risk factors and WAZ-GT classes.

Results: Four distinct classes of WAZ-GT were identified: maintaining WAZ > 0, 14%; stable around WAZ = 0, 35%; partially recovered, 28%; never recovered, 23%. Compared with reference group "stable around WAZ=0," we identified clinical and sociodemographic determinants of class membership for the three remaining groups. "Maintaining WAZ > 0" had greater odds of having biventricular physiology, borderline appetite, and a parent with at least a college education. "Partially recovered" had greater odds of hospital length of stay>14 days and being a single child in the household. "Never recovered" had greater odds hospital length of stay >14 and > 30 days, tube feeding at discharge, and low appetite.

Conclusions: This study described distinct classes of WAZ-GT for infants with cCHD early in infancy and identified associated determinants.

Practice implications: Findings from this study can be used in the identification of infants at risk of poor WAZ-GT and in the design of interventions to target growth in this vulnerable patient population.

Introduction

Infants born with complex congenital heart disease (cCHD), who require intervention in the first weeks of life for survival, are at increased risk for poor growth (Anderson et al., 2011; Burch et al., 2014; Costello et al., 2015; Daymont et al., 2013; Hansson et al., 2016; Ross et al., 2020). Low weight-for-age *Z*-score (WAZ) and length-for-age *Z*-score are associated with increased mortality and morbidities (Mitting et al., 2015; Ross et al., 2020), including worse neurodevelopmental outcomes after neonatal surgery (Medoff-Cooper et al., 2011; Ravishankar et al.,

Abbreviations: cCHD, complex congenital heart disease; LOS, length of stay; WAZ, weight-for-age *Z*-score; WAZ-GT, weight-for-age *Z*-score growth trajectory.

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2013). Prior studies have identified factors associated with poor growth in cCHD, including underlying genetic factors, the need for reintubation, and longer hospital length of stay (LOS) (Burnham et al., 2010; Costello et al., 2015; Hapuoja et al., 2021). Physiologic changes associated with cCHD may also influence growth, including alterations in resting energy expenditure (Kuip et al., 2007; Nydegger et al., 2009) and suppression of insulin-like growth factors (Avitabile et al., 2015; Chung et al., 2017; Surmeli-Onay et al., 2011). The provision of macro and micronutrients is critically important and poor growth has been associated with delays in the provision of postoperative nutrition (Anderson et al., 2011), the need for enteral tube feeding (Di Maria et al., 2013; Hsieh et al., 2019; Steward et al., 2020), and the presence of a feeding difficulty diagnosed by a speech language pathologist (Costello et al., 2015).

Deficits in growth trajectory over the first 36 months of life have been observed in children with cCHD when compared with healthy controls (Daymont et al., 2013). Different growth trajectories may exist within the cCHD population in the early postoperative period but these have not been defined. Growth trajectories may be influenced by many factors, which could shed light on new nursing interventions or target treatment approaches. The purposes of this study were to:

1. describe the growth trajectory of infants after neonatal cardiac surgery in the first 4 months of life;
2. determine if differences exist in the growth trajectory based on single or two ventricle physiology; and.
3. identify determinants of growth trajectory from sociodemographic factors and clinical characteristics.

Methods

We utilized data from a previously reported randomized clinical trial of the REACH telehealth home monitoring program in 2012–2017 (Trial Registration NCT01941667) (Medoff-Cooper et al., 2020). The REACH intervention provided parents with a structured telehealth program, including a daily text message, e-mail, or phone call and twice per week videoconferencing with an advanced practice nurse for 4 months after hospital discharge or until readmission for second stage surgery for infants with single ventricle (SV). Infants and their parents were recruited from three pediatric cardiac centers in the US. Parents provided informed consent for themselves and their infants prior to being enrolled in the trial. Infants with SV and two-ventricle were randomized to either the intervention or usual care. Usual care for the infants with SV was a home monitoring program at each participating center and for the infants with two ventricle physiology was a follow-up visit within 2 weeks after hospital discharge. The trial was approved by each institution's ethics review boards. The main study enrolled parent-infant dyads of infants with cCHD who had undergone cardiac surgery in the first three weeks of life. Eligibility criteria included infants who were at least 37 weeks gestation, weighed at least 2500 g at birth, and had a cCHD with a Risk Adjustment in Congenital Heart Surgery (RACHS-1) Mortality Category (Al-Radi et al., 2007) of at least 2. Exclusion criteria included infants with known genetic disorders and other syndromes (except for non-syndromic appearing DiGeorge syndrome), cardiomyopathy and/or those awaiting heart transplant. Additionally, the study excluded parents who did not speak or read English, were less than 18 years of age, and who did not have a cellphone or home Internet access. Demographic and clinical data were collected from infant medical records during the neonatal hospitalization. As a part of the (REACH) trial, all families in both intervention and control groups were discharged from the hospital with a digital scale and instructed to record their infant's weight daily. Additionally, parents completed surveys prior to the infant's hospital discharge and at 4 months post-discharge follow-up. The sample for the current study included all 178 infants from the main trial, including both intervention and control groups, as groups did not significantly differ in any of the current study's variables of interest.

Measures

Infant growth

Infant weight was converted to WAZ using the World Health Organization standards (de Onis et al., 2009). We included weekly WAZs up to 20 weeks (4 months) after birth, as this period includes a critical early timeframe of infant growth and ends at the time of the second stage of surgical palliation in infants with functional single ventricles.

The following variables were included as potential covariates for this study:

Demographic factors

Infant sex, race, ethnicity, prenatal vs postnatal cardiac diagnosis, and location of follow-up care were included as potential covariates. Additionally, the following family demographic variables were included as potential covariates: insurance type, number of children in household, parental education level, household income level, and number of parents in the household (mother and father, mother primarily, or mother + other). Finally, even though the (REACH) trial did not demonstrate significant infant or parent outcomes (Medoff-Cooper et al., 2020), the trial group assignment (intervention vs control) was tested for its potential effect on growth, but there was no significant difference found between groups.

Severity of illness/acuity

To capture infant acuity and severity of illness, the following available variables were extracted from the dataset and included in the analysis: RACHS-1 Mortality Category, type of cCHD (single ventricle vs two ventricle physiology), use of extracorporeal membrane oxygenation (ECMO), hospital length of stay (LOS), and rehospitalization.

Feeding variables

Feeding variables included history of infant preoperative oral feeding and feeding mode at discharge (oral only vs. tube fed exclusively or for supplementary nutrition). Parents completed the Millennium Infant Study Questionnaire (MISQ) (Tully et al., 2019; Wright et al., 2006; Wright et al., 2007) either at hospital discharge or study end to report on infant appetite, oromotor dysfunction, avoidant eating behavior, maternal feeding anxiety, and the extent to which the infant needed to be encouraged to finish the meal.

Analysis

Descriptive statistics were used to summarize the characteristics of infants and their families. To identify distinct growth trajectories, we used latent class growth modeling (LCGM), a semi-parametric technique to classify individuals following a similar pattern of WAZ change over time (Andruff et al., 2009; Becnel & Williams, 2019; Mattsson et al., 2019). LCGM summarizes the heterogeneity in individual WAZ growth in each class using a finite set of unique polynomial functions. The intercept and slope in each class are equally fixed across individuals in LCGM. A model with four trajectories of infant WAZ during the first 4 months demonstrated the best fit (Bayesian Information Criterion, BIC = −1520.44). BIC is a criterion for model selection among a finite set of models. Models with lower BIS are preferred. The average posterior probability of membership was high for all classes (range: 0.88–0.96) and above the suggested threshold of 0.8, indicating high reliability (Mo & Bodner, 2007). Stratified analysis by single or two ventricle physiology consistently yielded four trajectories with the best model fit.

To identify infant and family characteristics associated with infant WAZ growth trajectories over the first 4 months, we first tested their differences across the four WAZ trajectory classes using chi-square test, Fisher's exact test and ANOVA, and selected key characteristics with a p-value <0.2. As most of the diagnostic and follow-up care characteristics are closely linked to each other with a high level of collinearity, we examined their associations with WAZ growth trajectories independently using multinomial logistic regression models (Van Horn et al., 2008). The "stable around WAZ = 0" class was assigned as a reference group. All statistical analyses were done using Stata 16 (StataCorp LLC, College Station, TX) and SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

All 178 infants included in the final sample of the REACH study were included in this analysis. Most of the infants were White, non-Hispanic, living with both a mother and a father and on a private insurance policy (Table 1). The infants' parents reported a range of income and education levels, and a little more than half reported other children in the family in addition to the infant with cCHD. Most of the infants were prenatally diagnosed with cCHD and approximately half were diagnosed with a single ventricle type cCHD. RACHS-1 Mortality Categories ranged from 2 to 6 with nearly 40% belonging to category 6. Infant average birth weight was 3352 g (SD = 436) with an average WAZ at birth around zero (mean = 0.07, SD = 0.88). Mean LOS was approximately three weeks. About three-quarters of the infants had a LOS of at least 14 days, with less than one-quarter having a LOS of at least 30 days. At the time of discharge, nearly half were orally fed, and of the remainder, nearly a tenth exclusively tube fed.

Identification of infant WAZ growth trajectories

Latent class growth modeling identified four classes of distinct WAZ trajectories in our sample (Fig. 1). The class, "stable around WAZ = 0" ($n = 63$, 35.4%), is characterized by a birth WAZ around 0, which drops after birth but slowly regains, approaching the WAZ at birth. The class, "maintaining WAZ > 0" ($n = 25$, 14%) is characterized by a birth WAZ >1, with a drop in WAZ after birth, but the mean WAZ remains >0, and demonstrates a positive WAZ trajectory through 4 months after the initial drop. The "partially-recovered" class ($n = 49$, 27.5%) is characterized by a WAZ at birth <0, a pronounced drop in WAZ after birth but regain afterward, not reaching the WAZ at birth. The "never-recovered" class ($n = 41$, 23.0%) is characterized by a WAZ at birth <0, a pronounced drop in WAZ after birth, with a continuing drop in WAZ to <−2 at the first 4 months. Comparisons of infant growth trajectories by ventricular physiology found no significant differences; meaning, the distributions of 4 classes of WAZ-GT were not different by ventricular physiology ($p = 0.11$; Fig. 2). We also compared infant growth trajectories by (REACH) trial randomized group assignment (intervention vs. control) and found no significant differences ($p = 0.37$).

Infant and family characteristics associated with trajectory class

Clinical and sociodemographic characteristics were significantly associated with odds of membership in a class other than "stable around WAZ = 0" (Table 2). Specifically, infants in the "never-recovered" class, compared with the "stable around WAZ = 0" class, were more likely to have LOS 14 days or greater, LOS 30 days or greater, tube feeding at discharge, oral and tube feeding at discharge and low appetite. Infants in the "partially-recovered" class were three times more likely to have a LOS 14 days or greater and being a single child in the household, compared with "stable around WAZ = 0" class. Finally, infants were more likely to be in class "maintaining WAZ > 0" compared with "stable

Table 1
Infant and family clinical and sociodemographic characteristics, $n = 178$.

	n(%) or mean(SD)
Female Sex	73 (41%)
White Race	141 (79%)
Hispanic Ethnicity	15 (8%)
RACHS-1 Mortality Category	
2	16 (9%)
3	60 (34%)
4	31 (17%)
5	3 (2%)
6	68 (38%)
Single-ventricle-type cCHD	95 (53%)
Timing of cardiac diagnosis - Prenatal	143 (80%)
Birth weight in grams, mean (SD)	3352 (436)
Weight-for-Age Z-Score (WAZ) at Birth, mean (SD)	0.07 (0.88)
ECMO	1 (1%)
Hospital length of stay	
Total, mean (SD)	23 (14)
Hospital length of stay: 14 days or more	131 (74%)
Hospital length of stay: 30 days or more	39 (22%)
Discharged on digoxin	49 (28%)
Preoperative oral feeding	125 (70%)
Feeding mode at discharge	
Oral feeding only	87 (49%)
Tube and oral feeding	77 (43%)
Tube feeding only	14 (8%)
Ever re-hospitalized	76 (43%)
Place of receiving follow-up care	
Center where surgery performed	127 (71%)
Another center only	13 (7%)
Both	38 (21%)
Insurance type	
Private	127 (71%)
vNon-private/government funded	51 (29%)
Number of children in household	
1	72 (40%)
2+	106 (60%)
Family status*	
Both parents	166 (94%)
Mother primarily	10 (6%)
Mother and Other	1 (1%)
Parental education level*	
Partial/graduated from high school or partial college	55 (36%)
Graduated college	96 (64%)
Household income level*	
$0-49,999	50 (36%)
$50,000-99,999	45 (32%)
$100,000+	45 (32%)
Millennium Infant Study Questionnaire (MISQ)	
1. Appetite*	
Normal	82 (47%)
Borderline	55 (32%)
Low	37 (21%)
2. Oromotor dysfunction*	
Normal	55 (32%)
Borderline	52 (30%)
Low	66 (30%)
3. Avoidant eating behavior*	
Low	69 (40%)
Medium	79 (46%)
High	25 (15%)
4. Maternal feeding anxiety*	
Normal	1 (1%)
Borderline	9 (5%)
High	164 (94%)
5. Encourage child to finish the meal*	
Low	23 (13%)
Medium	60 (35%)
High	90 (52%)

Data reported as count (percent) or mean (standard deviation).
cCHD-critical congenital heart disease.
RACHS- Risk Adjustment in Congenital Heart Surgery.
WAZ-GT: weight-for-age Z-score growth trajectory.
* The sample sizes different by variables due to missing data.

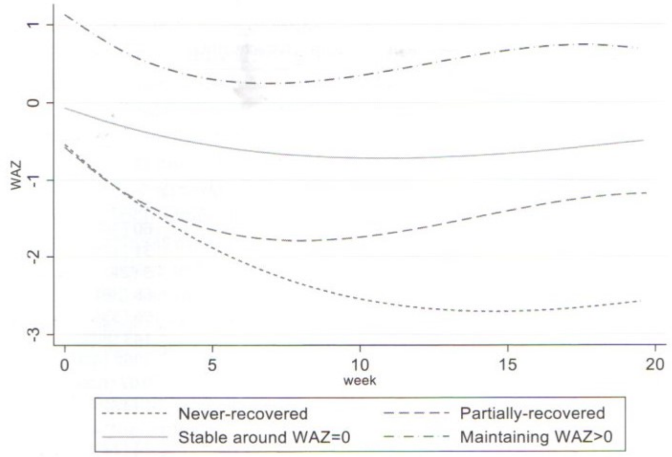

Fig. 1. Infant growth trajectory classes.

around WAZ = 0" class if they had two ventricle physiology and a parent with at least a college education. Additionally, infants with borderline appetites had a smaller chance to be in this group than infants with a normal appetite.

Discussion

This study used latent class analysis to identify 4 classes of growth trajectory in infants with cCHD. Interesting, all classes experienced a drop in WAZ from birth to discharge. This finding is consistent with other studies that have demonstrated a pronounced drop in WAZ after neonatal cardiac surgery (Hsu et al., 2010). Approximately half of the infants fell into the poor growth trajectory classes ("partially-recovered" and "never-recovered"), and only 14% demonstrated "maintaining WAZ > 0" by 4 months. One important element to class membership was birth WAZ. Other studies have demonstrated that preoperative nutritional status as measured by birth WAZ strongly influences subsequent growth (Burch et al., 2014; Hapuoja et al., 2021; Shi et al., 2020; Vaidyanathan et al., 2009) and is an independent risk factor for adverse outcomes, including mortality (Mitting et al., 2015; Ross et al., 2020; Steurer et al., 2021). Our study similarly showed that infants in the poor growth trajectories start with a lower birth WAZ compared to those in the positive growth trajectories.

None of the classes of growth trajectory returned to birth WAZ by 4 months post-discharge. This raises important questions about what the expected trajectory should be for these extremely vulnerable infants with cCHD. Infants in classes "stable around WAZ=0" and "maintaining WAZ > 0" remained within or above population norms. While none of the infants in any of the classes returned to their at-birth WAZ by 4 months of life, about one-quarter of infants, who were in the "never-recovered" group demonstrated persistent growth failure with WAZ < −2 at 4 months. Persistent growth failure as measured by WAZ was also found in approximately one-quarter of infants with CHD in a recent study at 6 months of life (Steward et al., 2020) and in one-quarter of infants from another cross-sectional study examining WAZ across the first two years of life (Monteiro et al., 2012). Studies have also demonstrated that growth failure may persist in a percentage of children with cCHD even at 3 (Burch et al., 2014) and 4 (Burnham et al., 2010) years of age.

For our second aim, we found no differences in growth trajectory based on type of cCHD. When performing latent class analysis separately in the single and two ventricle infants, the same four classes were identified. Also, the distribution of four classes defined in the total sample were not significantly different by type of cCHD. These findings are supported by other studies which have examined whether differences in growth exist between cyanotic and acyanotic CHD (Costello et al., 2015) or between single and two ventricle cCHD (Ross et al., 2020) and found no differences. Some studies have classified infants with cCHD into groups based on clinical indicators such as presence of pulmonary hypertension or cyanosis to compare growth outcomes (Blasquez et al., 2016). One study on growth trajectory of infants found that complexity of CHD significantly influenced growth trajectory outcomes (Shi et al., 2020) However, that study's definition of CHD complexity was not determined by any standardized or previously studied defect categories (Gaynor et al., 2015; International Cardiac Collaborative on Neurodevelopment, I, 2016) or surgical categories, such as STAT (O'Brien et al., 2009) or RACHS-1 (Al-Radi et al., 2007). We did find, however, that infants with two ventricle physiology were more likely to be in "maintaining WAZ > 0" compared to "stable around WAZ=0". More research is needed to determine the influence of complexity or type of cCHD on growth trajectory.

The multinomial logistic regression predicting membership of classes provides new insights into variables that may explain past heterogeneity of outcomes and previously unknown associations. Infants were more likely to be in "partially-recovered" and "never-recovered" compared with "stable around WAZ=0" if they had a prolonged LOS. LOS is often regarded as a proxy for medical complexity and severity of

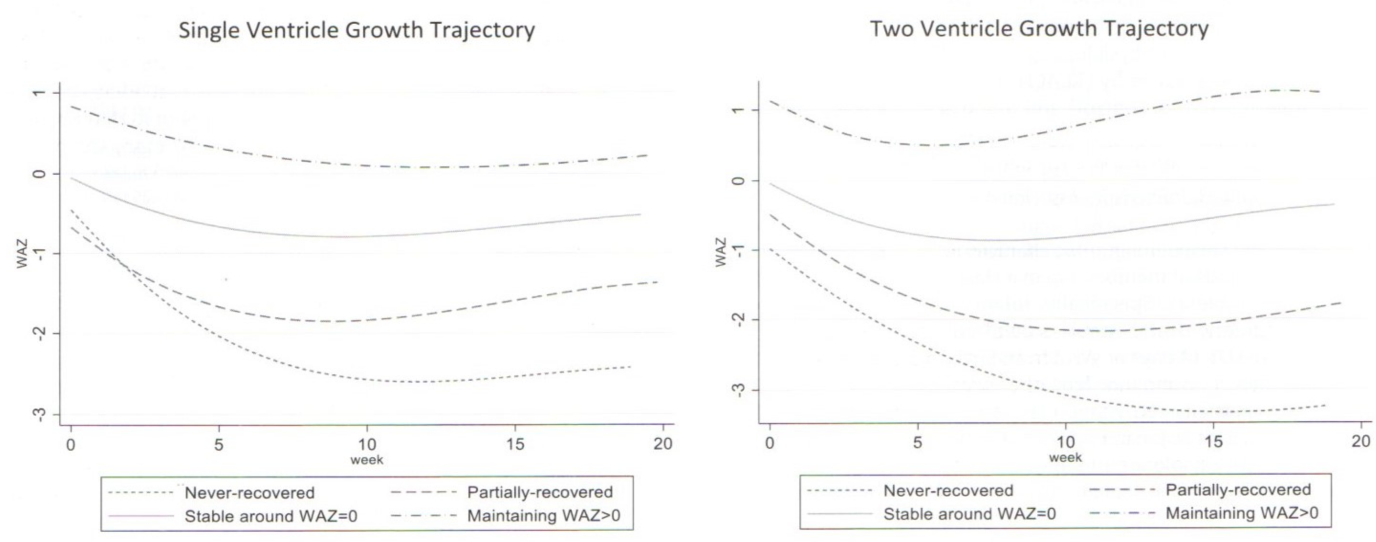

Fig. 2. Infant growth trajectory classes stratified by single and two ventricle cCHD.

Table 2
Multinomial logistic regression models by growth trajectory class.

Reference Class: "Stable around WAZ = 0"	Odds Ratio (95% Confidence Interval)	*p*-value
CLASS "NEVER-RECOVERED"		
Hispanic (ref: non-Hispanic)	4.12 (0.99, 16.97)	0.05
Two ventricle physiology (ref: Single ventricle)	1.31 (0.59, 2.91)	0.50
Prenatal cardiac diagnosis (ref: Postnatal)	1.26 (0.46, 3.49)	0.65
Hospital length of stay		
14d + hospital stay (ref: <14d)	**3.35 (1.23, 9.18)**	**0.01**
30d + hospital stay (ref: <30d)	**9.05 (3.20, 25.61)**	**<0.001**
Feeding mode at discharge (ref: oral feeding only)	**3.13 (1.28, 7.65)**	**0.01**
Tube + oral feeding at discharge	**6.55 (1.65, 25.94)**	**0.007**
Tube feeding only at discharge		
A single child in the household (ref: multiple children)	0.87 (0.38, 2.00)	0.73
Parent with at least college education (ref: less educated)	0.99 (0.43, 2.31)	0.98
MISQ-appetite (ref: normal)		
Borderline	1.53 (0.59, 3.98)	0.37
Low	**3.44 (1.18, 10.04)**	**0.02**
CLASS "PARTIALLY-RECOVERED"		
Hispanic (ref: non-Hispanic)	1.30 (0.25, 6.76)	0.75
Two ventricle physiology (ref: Single ventricle)	1.24 (0.58, 2.64)	0.57
Prenatal cardiac diagnosis (ref: Postnatal)	1.86 (0.65, 5.32)	0.24
Hospital length of stay		
14d + hospital stay (ref: <14d)	**2.95 (1.18, 7.36)**	**0.02**
30d + hospital stay (ref: <30d)	2.44 (0.82, 7.25)	0.10
Feeding mode at discharge (ref: oral feeding only)	1.26 (0.58, 2.75)	0.55
Tube + oral feeding at discharge	0.69 (0.12, 4.07)	0.68
Tube feeding only at discharge		
A single child in the household (ref: multiple children)	**2.70 (1.25, 5.84)**	**0.01**
Parent with at least college education (ref: less educated)	0.91 (0.39, 2.13)	0.82
MISQ-appetite (ref: normal)		
Borderline	0.54 (0.23, 1.28)	0.16
Low	0.80 (0.27, 2.34)	0.68
CLASS "MAINTAINING WAZ > 0"		
Hispanic (ref: non-Hispanic)	1.74 (0.27, 11.09)	0.55
Two ventricle physiology (ref: Single ventricle)	**3.23 (1.21, 8.61)**	**0.01**
Prenatal cardiac diagnosis (ref: Postnatal)	0.46 (0.17, 1.28)	0.13
Hospital length of stay		
14d + hospital stay (ref: <14d)	0.86 (0.33, 2.23)	0.76
30d + hospital stay (ref: <30d)	1.30 (0.30, 5.64)	0.73
Feeding mode at discharge (ref: oral feeding only)	1.23 (0.48, 3.17)	0.66
Tube + oral feeding at discharge	N/A*	
Tube feeding only at discharge		
A single child in the household (ref: multiple children)	0.88 (0.33, 2.35)	0.79
Parent with at least college education (ref: less educated)	**3.88 (1.02, 14.73)**	**0.04**
MISQ-appetite (ref: normal)		
Borderline	**0.20 (0.05, 0.76)**	**0.01**
Low	0.79 (0.23, 2.73)	0.71

Bold $p < 0.05$. Separate multinomial logistic regression models were used for each diagnostic and follow-up care characteristic.
MISQ-Millennium Infant Study Questionnaire.
WAZ- weight-for-age Z-score growth trajectory.
* N/A = not applicable due to no tube fed only infants in Class "Maintaining WAZ > 0".

illness. The Pediatric Heart Network Single Ventricle trial found that LOS of infants predicted change in WAZ from birth to 3 years of age (Burch et al., 2014). They also found that other severity of illness indicators such as tricuspid valve regurgitation negatively influenced WAZ change. It would appear that LOS has a similar influence over growth trajectory for infants with a prolonged LOS most likely to fall into the worse growth trajectories of "never" or "partially" recovered. Perhaps opportunities exist to optimize the delivery of nutrition during infant hospitalization, particularly in infants with prolonged LOS. Delays in the delivery of post-operative nutrition have been demonstrated to be associated with lower WAZ score (Anderson et al., 2011). Variation in growth outcomes has been demonstrated within and across centers caring for infants with cCHD, with centers that provide more standardized nutrition management demonstrating improved growth outcomes (Anderson et al., 2012; Lisanti et al., 2021). Standardized feeding pathways have demonstrated some improvements in growth, but it is unknown whether these improvements result in substantial differences in growth trajectory over time. If the provision of nutrition during the hospital stay could mitigate the profound loss of WAZ from birth to hospital discharge, perhaps the trajectory of growth over time would be influenced as well.

Infants who received tube feeding at discharge were more likely to be in "never-recovered" versus "stable around WAZ=0." This was not a surprising finding since past research has demonstrated that orally fed infants have better growth outcomes at 6, 12, and 24 months than those fed by tube (Butto et al., 2019; Steward et al., 2020). Of note, the "never-recovered" class was also more likely to have infants with a parent report of low appetite and "maintaining WAZ > 0" was less likely to have infants with parent report of a borderline appetite. Therefore, infants with normal appetite had a greater chance to have a stable growth trajectory, compared to infants with low or borderline appetite. It may be that the feeding tube is not in itself the issue, but a marker for other variables including severity of illness and perhaps even appetite. Infants who do not demonstrate feeding cues, who cannot attain a prolonged awake, attentive state, or who tire easily often have a feeding tube placed to supplement nutrition that is unable to be provided solely through oral means. This is the first study to incorporate appetite as a contributing variable to growth outcomes in cCHD. More research is needed regarding the role of feeding tubes in augmenting the provision of nutrition to infants with cCHD and other interventions that may support oral feeding in infants with low appetite.

Finally, sociodemographic variables were also found to be predictive of growth trajectory class. Parent education level influenced infant growth trajectory. Specifically, infants whose parents had at least a college education were four times more likely to be in the class "maintaining WAZ > 0" than "stable around WAZ=0." Maternal education has been found to be protective of growth faltering in infants with other chronic illnesses, such as HIV infection (Webb et al., 2009). The effect of number of children in the home was a surprising finding in that infants who were a single child were more likely to be in "partially-recovered" compared with "stable around WAZ = 0." We might have expected that parents with other children would be more stressed or busy with competing responsibilities resulting in a negative impact on their ability to feed or monitor growth in their infants. However, perhaps experience as a parent of other children has some influence. Possibly providing new parents with more education on infant feeding behaviors or parenting would be beneficial. This study is the first to identify sociodemographic variables, such as maternal education and number of children in the home, as determinants of growth trajectory of infants with cCHD. Future studies on growth trajectory should include these variables and develop targeted interventions to support these at-risk groups.

Practice implications

Nurses caring for infants with cCHD have a key role in the measurement of infant weight and in closely monitoring growth over time, and this is especially important for the at-risk infants identified in this study. All infants with cCHD need regular and frequent anthropometrics assessed during their hospitalization, through their recovery after cardiac surgery, and post-discharge (Medoff-Cooper & Ravishankar, 2013). Nurses can also support the provision of adequate nutrition during these periods of early growth. Nurses can target early and standardized nutrition therapy both in the pre- and postoperative periods of the infants' hospitalization, particularly for those infants with a birth WAZ less than zero and those requiring a feeding tube.

Additionally, nurses can connect families with post-discharge support from a registered dietitian and feeding specialist to provide the early intervention critically needed for these at-risk groups (Slicker et al., 2013). Nurses are also poised to assess families for their educational needs and available resources regarding their infants' nutritional and feeding needs. Nurses can provide focused education for new mothers and tailored learning opportunities for families needing additional support.

Limitations

The secondary analysis of data that were previously collected for the randomized trial limited our ability to include additional variables. We did not have access to caloric or nutritional data beyond feeding mode at discharge that may have influenced growth trajectory. Height/Length-for age Z-score and head circumferences are important anthropometrics that were not available for this analysis (Cohen et al., 2010; Lambert et al., 2020). Additionally, we only had data through the first 4 months post-discharge. Growth trajectories may continue to evolve throughout early childhood.

Conclusion

This study is the first to describe distinct classes of growth trajectory for infants with cCHD over the first 4 months of life and to identify determinants of class membership. Findings from this study can be used by nurses in the identification of infants at risk of poor growth trajectory and in the design of interventions to target growth in this vulnerable patient population. Future studies would be strengthened by strategically enrolling more diverse samples, representing more racial and ethnic groups with a wider range of socioeconomic status and location. Research is needed to identify long-term outcomes of each of the four classes we identified in this study.

Disclosure statement

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Declarations of interest

None.

Author contributions

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References

Al-Radi, O. O., Harrell, F. E., Jr., Caldarone, C. A., McCrindle, B. W., Jacobs, J. P., Williams, M. G., ... Williams, W. G. (2007, Apr). Case complexity scores in congenital heart surgery: A comparative study of the aristotle basic complexity score and the risk adjustment in congenital heart surgery (RACHS-1) system. *The Journal of Thoracic and Cardiovascular Surgery*, *133*(4), 865–875. https://doi.org/10.1016/j.jtcvs.2006.05.071.

Anderson, J. B., Iyer, S. B., Schidlow, D. N., Williams, R., Varadarajan, K., Horsley, M., ... National Pediatric Cardiology Quality Improvement, C (2012, Jul). Variation in growth of infants with a single ventricle. *The Journal of Pediatrics*, *161*(1), 16–21 e11; quiz 21 e12–13 https://doi.org/10.1016/j.jpeds.2012.01.009.

Anderson, J. B., Marino, B. S., Irving, S. Y., Garcia-Espana, J. F., Ravishankar, C., Stallings, V. A., & Medoff-Cooper, B. (2011, Aug). Poor post-operative growth in infants with two-ventricle physiology. *Cardiology in the Young*, *21*(4), 421–429. https://doi.org/10.1017/S1047951111000229.

Andruff, H., Carraro, N., Thompson, A., Gaudreau, P., & Louvet, B. (2009). Latent class growth modelling: A tutorial. *Tutorial in Quantitative Methods for Psychology*, *5*(1), 11–24. https://doi.org/10.20982/tqmp.05.1.p011.

Avitabile, C. M., Leonard, M. B., Brodsky, J. L., Whitehead, K. K., Ravishankar, C., Cohen, M. S., ... Goldberg, D. J. (2015, Mar 15). Usefulness of insulin like growth factor 1 as a marker of heart failure in children and young adults after the Fontan palliation procedure. *The American Journal of Cardiology*, *115*(6), 816–820. https://doi.org/10.1016/j.amjcard.2014.12.041.

Becnel, J. N., & Williams, A. L. (2019, Nov). Using latent class growth modeling to examine longitudinal patterns of body mass index change from adolescence to adulthood. *Journal of the Academy of Nutrition and Dietetics*, *119*(11), 1875–1881. https://doi.org/10.1016/j.jand.2019.04.025.

Blasquez, A., Clouzeau, H., Fayon, M., Mouton, J. B., Thambo, J. B., Enaud, R., & Lamireau, T. (2016, Apr). Evaluation of nutritional status and support in children with congenital heart disease. *European Journal of Clinical Nutrition*, *70*(4), 528–531. https://doi.org/10.1038/ejcn.2015.209.

Burch, P. T., Gerstenberger, E., Ravishankar, C., Hehir, D. A., Davies, R. R., Colan, S. D., ... Pediatric Heart Network, I (2014, Jun 23). Longitudinal assessment of growth in hypoplastic left heart syndrome: Results from the single ventricle reconstruction trial. *Journal of the American Heart Association*, *3*(3), Article e000079. https://doi.org/10.1161/JAHA.114.000079.

Burnham, N., Ittenbach, R. F., Stallings, V. A., Gerdes, M., Zackai, E., Bernbaum, J., ... Gaynor, J. W. (2010, Jul). Genetic factors are important determinants of impaired growth after infant cardiac surgery. *The Journal of Thoracic and Cardiovascular Surgery*, *140*(1), 144–149. https://doi.org/10.1016/j.jtcvs.2010.01.003.

Butto, A., Mercer-Rosa, L., Teng, C., Daymont, C., Edelson, J., Faerber, J., ... Cohen, M. S. (2019, Nov). Longitudinal growth in patients with single ventricle cardiac disease receiving tube-assisted feeds. *Congenital Heart Disease*, *14*(6), 1058–1065. https://doi.org/10.1111/chd.12843.

Chung, H. T., Chang, Y. S., Liao, S. L., & Lai, S. H. (2017, Apr). The effects of corrective surgery on endothelial biomarkers and anthropometric data in children with congenital heart disease. *The Journal of International Medical Research*, *45*(2), 493–503. https://doi.org/10.1177/0300060516685659.

Cohen, M. S., Zak, V., Atz, A. M., Printz, B. F., Pinto, N., Lambert, L., ... McCrindle, B. W. (2010, Dec). Anthropometric measures after Fontan procedure: Implications for suboptimal functional outcome. *American Heart Journal*, *160*(6), 1092–1098 1098 e1091 https://doi.org/10.1016/j.ahj.2010.07.039.

Costello, C. L., Gellatly, M., Daniel, J., Justo, R. N., & Weir, K. (2015, Sep-Oct). Growth restriction in infants and young children with congenital heart disease. *Congenital Heart Disease*, *10*(5), 447–456. https://doi.org/10.1111/chd.12231.

Daymont, C., Neal, A., Prosnitz, A., & Cohen, M. S. (2013, Jan). Growth in children with congenital heart disease. *Pediatrics*, *131*(1), e236–e242. https://doi.org/10.1542/peds.2012-1157.

Di Maria, M. V., Glatz, A. C., Ravishankar, C., Quartermain, M. D., Rush, C. H., Nance, M., ... Goldberg, D. J. (2013, Aug). Supplemental tube feeding does not mitigate weight loss in infants with shunt-dependent single-ventricle physiology. *Pediatric Cardiology*, *34*(6), 1350–1356. https://doi.org/10.1007/s00246-013-0648-x.

Gaynor, J. W., Stopp, C., Wypij, D., Andropoulos, D. B., Atallah, J., Atz, A. M., ... McQuillen, P. S.International Cardiac Collaborative on Neurodevelopment, I. (2015, May). Neurodevelopmental outcomes after cardiac surgery in infancy. *Pediatrics*, *135*(5), 816–825. https://doi.org/10.1542/peds.2014-3825.

Hansson, L., Ohlund, I., Lind, T., Stecksen-Blicks, C., & Rydberg, A. (2016, Feb). Dietary intake in infants with complex congenital heart disease: A case-control study on macro- and micronutrient intake, meal frequency and growth. *Journal of Human Nutrition and Dietetics*, *29*(1), 67–74. https://doi.org/10.1111/jhn.12285.

Hapuoja, L., Kretschmar, O., Rousson, V., Dave, H., Naef, N., & Latal, B. (2021, May). Somatic growth in children with congenital heart disease at 10 years of age: Risk factors and longitudinal growth. *Early Human Development*, *156*, Article 105349. https://doi.org/10.1016/j.earlhumdev.2021.105349.

Hsieh, A., Tabbutt, S., Xu, D., Barkovich, A. J., Miller, S., McQuillen, P., & Peyvandi, S. (2019, May 21). Impact of perioperative brain injury and development on feeding modality in infants with single ventricle heart disease. *Journal of the American Heart Association*, *8*(10), Article e012291. https://doi.org/10.1161/JAHA.119.012291.

Hsu, D. T., Zak, V., Mahony, L., Sleeper, L. A., Atz, A. M., Levine, J. C., ... Pediatric Heart Network, I. (2010, Jul 27). Enalapril in infants with single ventricle: Results of a multicenter randomized trial. *Circulation, 122*(4), 333–340. https://doi.org/10.1161/CIRCULATIONAHA.109.927988.

International Cardiac Collaborative on Neurodevelopment, I. (2016, Sep). Impact of operative and postoperative factors on neurodevelopmental outcomes after cardiac operations. *The Annals of Thoracic Surgery, 102*(3), 843–849. https://doi.org/10.1016/j.athoracsur.2016.05.081.

Kuip, M., Hoos, M. B., Forget, P. P., Westerterp, K. R., Gemke, R., Meer, K., & d. (2007). Energy expenditure in infants with congenital heart disease, including a meta-analysis. *Acta Paediatrica, 92*(8), 921–927. https://doi.org/10.1111/j.1651-2227.2003.tb00625.x.

Lambert, L. M., McCrindle, B. W., Pemberton, V. L., Hollenbeck-Pringle, D., Atz, A. M., Ravishankar, C., ... Pediatric Heart Network, I (2020, Jun). Longitudinal study of anthropometry in Fontan survivors: Pediatric Heart Network Fontan study. *American Heart Journal, 224*, 192–200. https://doi.org/10.1016/j.ahj.2020.03.022.

Lisanti, A. J., Savoca, M., Gaynor, J. W., Mascarenhas, M. R., Ravishankar, C., Sullivan, E., ... Irving, S. Y. (2021, Apr). Standardized feeding approach mitigates weight loss in infants with congenital heart disease. *The Journal of Pediatrics, 231*, 124–130 e121. https://doi.org/10.1016/j.jpeds.2020.12.047.

Mattsson, M., Maher, G. M., Boland, F., Fitzgerald, A. P., Murray, D. M., & Biesma, R. (2019, Jul). Group-based trajectory modelling for BMI trajectories in childhood: A systematic review. *Obesity Reviews, 20*(7), 998–1015. https://doi.org/10.1111/obr.12842 (Citation Blinded for Peer Review).

Medoff-Cooper, B., Irving, S. Y., Marino, B. S., Garcia-Espana, J. F., Ravishankar, C., Bird, G. L., & Stallings, V. A. (2011, Apr). Weight change in infants with a functionally univentricular heart: From surgical intervention to hospital discharge. *Cardiology in the Young, 21*(2), 136–144. https://doi.org/10.1017/S104795111000154X.

Medoff-Cooper, B, Marino, B. S., Fleck, D. A., Lisanti, A. J., Golfenshtein, N., Ravishankar, C., & Curley, M. A. Q. (2020). Telehealth Home Monitoring and Postcardiac Surgery for Congenital Heart Disease. *Pediatrics, 146*(3), e20200531. https://doi.org/10.1542/peds.2020-0531.

Medoff-Cooper, B., & Ravishankar, C. (2013, Mar). Nutrition and growth in congenital heart disease: A challenge in children. *Current Opinion in Cardiology, 28*(2), 122–129. https://doi.org/10.1097/HCO.0b013e32835dd005.

Mitting, R., Marino, L., Macrae, D., Shastri, N., Meyer, R., & Pathan, N. (2015, Jun). Nutritional status and clinical outcome in postterm neonates undergoing surgery for congenital heart disease. *Pediatric Critical Care Medicine, 16*(5), 448–452. https://doi.org/10.1097/PCC.0000000000000402.

Mo, W., & Bodner, T. E. (2007). Growth mixture modeling. *Organizational Research Methods, 10*(4), 635–656. https://doi.org/10.1177/1094428106289397.

Monteiro, F. P., de Araujo, T. L., Lopes, M. V., Chaves, D. B., Beltrao, B. A., & Costa, A. G. (2012, Nov-Dec). Nutritional status of children with congenital heart disease. *Revista Latino-Americana de Enfermagem, 20*(6), 1024–1032. https://doi.org/10.1590/s0104-11692012000600003.

Nydegger, A., Walsh, A., Penny, D. J., Henning, R., & Bines, J. E. (2009, Mar). Changes in resting energy expenditure in children with congenital heart disease. *European Journal of Clinical Nutrition, 63*(3), 392–397. https://doi.org/10.1038/sj.ejcn.1602956.

O'Brien, S. M., Clarke, D. R., Jacobs, J. P., Jacobs, M. L., Lacour-Gayet, F. G., Pizarro, C., ... Edwards, F. H. (2009, Nov). An empirically based tool for analyzing mortality associated with congenital heart surgery. *The Journal of Thoracic and Cardiovascular Surgery, 138*(5), 1139–1153. https://doi.org/10.1016/j.jtcvs.2009.03.071.

de Onis, M., Garza, C., Onyango, A. W., Rolland-Cachera, M. F., & le Comite de nutrition de la Societe francaise de, p (2009, Jan). WHO growth standards for infants and young children. *Archives de Pédiatrie, 16*(1), 47–53. https://doi.org/10.1016/j.arcped.2008.10.010 (Les standards de croissance de l'Organisation mondiale de la sante pour les nourrissons et les jeunes enfants.).

Ravishankar, C., Zak, V., Williams, I. A., Bellinger, D. C., Gaynor, J. W., Ghanayem, N. S., ... Pediatric Heart Network, I. (2013, Feb). Association of impaired linear growth and worse neurodevelopmental outcome in infants with single ventricle physiology: A report from the pediatric heart network infant single ventricle trial. *The Journal of Pediatrics, 162*(2), 250–256 e252 https://doi.org/10.1016/j.jpeds.2012.07.048.

Ross, F. J., Radman, M., Jacobs, M. L., Sassano-Miguel, C., Joffe, D. C., Hill, K. D., ... Latham, G. J. (2020, Jun). Associations between anthropometric indices and outcomes of congenital heart operations in infants and young children: An analysis of data from the Society of Thoracic Surgeons Database. *American Heart Journal, 224*, 85–97. https://doi.org/10.1016/j.ahj.2020.03.012.

Shi, H., Hu, C., Zhang, L., Tong, M., Li, L., & Cui, Y. (2020, Sep 11). Early growth trajectory of infants with simple congenital heart disease and complex congenital heart disease undergoing cardiac repair: A prospective cohort study in China. *JPEN Journal of Parenteral and Enteral Nutrition, 45*(6), 1181–1191. https://doi.org/10.1002/jpen.2017.

Slicker, J., Hehir, D. A., Horsley, M., Monczka, J., Stern, K. W., Roman, B., ... Feeding Work Group of the National Pediatric Cardiology Quality Improvement, C (2013, Mar-Apr). Nutrition algorithms for infants with hypoplastic left heart syndrome; birth through the first interstage period. *Congenital Heart Disease, 8*(2), 89–102. https://doi.org/10.1111/j.1747-0803.2012.00705.x.

Steurer, M. A., Peyvandi, S., Costello, J. M., Moon-Grady, A. J., Habib, R. H., Hill, K. D., & Rajagopal, S. (2021, Jan 29). Association between Z-score for birth weight and postoperative outcomes in neonates and infants with congenital heart disease. *The Journal of Thoracic and Cardiovascular Surgery, 162*(6), 1838–1847 e4 https://doi.org/10.1016/j.jtcvs.2021.01.065.

Steward, D. K., Ryan-Wenger, N., Harrison, T. M., & Pridham, K. F. (2020). Patterns of growth and nutrition from birth to 6 months in infants with complex congenital cardiac defects. *Nursing Research, 69*(5S Suppl 1), S57–S65 Sep/Oct https://doi.org/10.1097/NNR.0000000000000460.

Surmeli-Onay, O., Cindik, N., Kinik, S. T., Ozkan, S., Bayraktar, N., & Tokel, K. (2011). The effect of corrective surgery on serum IGF-1, IGFBP-3 levels and growth in children with congenital heart disease. *Journal of Pediatric Endocrinology & Metabolism, 24*(7–8), 483–487. https://doi.org/10.1515/jpem.2011.061.

Tully, L., Wright, C. M., McCormick, D., & Garcia, A. L. (2019, May 16). Assessing the potential for integrating routine data collection on complementary feeding to child health visits: A mixed-methods study. *International Journal of Environmental Research and Public Health, 16*(10). https://doi.org/10.3390/ijerph16101722.

Vaidyanathan, B., Radhakrishnan, R., Sarala, D. A., Sundaram, K. R., & Kumar, R. K. (2009, Aug). What determines nutritional recovery in malnourished children after correction of congenital heart defects? *Pediatrics, 124*(2), e294–e299. https://doi.org/10.1542/peds.2009-0141.

Van Horn, M. L., Fagan, A. A., Jaki, T., Brown, E. C., Hawkins, J. D., Arthur, M. W., ... Catalano, R. F. (2008). Using multilevel mixtures to evaluate intervention effects in group randomized trials. *Multivariate Behavioral Research, 43*(2), 289–326. https://doi.org/10.1080/00273170802034893.

Webb, A. L., Manji, K., Fawzi, W. W., & Villamor, E. (2009, Apr). Time-independent maternal and infant factors and time-dependent infant morbidities including HIV infection, contribute to infant growth faltering during the first 2 years of life. *Journal of Tropical Pediatrics, 55*(2), 83–90. https://doi.org/10.1093/tropej/fmn068.

Wright, C. M., Parkinson, K. N., & Drewett, R. F. (2006, Apr). How does maternal and child feeding behavior relate to weight gain and failure to thrive? Data from a prospective birth cohort. *Pediatrics, 117*(4), 1262–1269. https://doi.org/10.1542/peds.2005-1215.

Wright, C. M., Parkinson, K. N., Shipton, D., & Drewett, R. F. (2007, Oct). How do toddler eating problems relate to their eating behavior, food preferences, and growth? *Pediatrics, 120*(4), e1069–e1075. https://doi.org/10.1542/peds.2006-2961.